General

Guideline Title

Suspected cancer: recognition and referral.

Bibliographic Source(s)

National Collaborating Centre for Cancer. Suspected cancer: recognition and referral. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Jun 23. 95 p. (NICE guideline; no. 12).

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: National Collaborating Centre for Primary Care. Referral guidelines for suspected cancer in adults and children. London (UK): Royal College of General Practitioners; 2005 Jun. 791 p. [452 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Cancer (NCC-C) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

The following guidance is based on the best available evidence. The full version of the guideline gives details of the methods and the evidence used to develop the guidance.

The wording used in the recommendations in this guideline (for example, words such as 'offer' and 'consider') denotes the certainty with which the recommendation is made (the strength of the recommendation) and is defined at the end of the "Major Recommendations" field.

Recommendations are marked as [new 2015], [2015], [2011] or [2005]:

- [new 2015] indicates that the evidence has been reviewed and the recommendation has been added or updated
- [2015] indicates that the evidence has been reviewed but no change has been made to the recommended action
- [2005] [2011] indicates that the evidence has not been reviewed since that date (of the original guideline)

Recommendations Organised by Site of Cancer

The recommendations in this guideline have been organised into 3 separate sections to help healthcare professionals find the relevant information

easily. This section includes the recommendations for investigation and referral organised by the site of the suspected cancer. There is also a section (see below) covering patient support, safety netting and the diagnostic process, which should be used in conjunction with this section. The recommendations in this section have also been organised by symptoms and investigation findings in a separate section; see the original guideline document for this section.

Lung and Pleural Cancers

Lung Cancer

Recommendations in this section update recommendations 1.1.2 to 1.1.5 in NICE guideline CG121 (see Lung cancer. The diagnosis and treatment of lung cancer).

Refer people using a suspected cancer pathway referral (for an appointment within 2 weeks) for lung cancer if they:

- Have chest X-ray findings that suggest lung cancer or
- Are aged 40 and over with unexplained haemoptysis [new 2015]

Offer an urgent chest X-ray (to be performed within 2 weeks) to assess for lung cancer in people aged 40 and over if they have 2 or more of the following unexplained symptoms, or if they have ever smoked and have 1 or more of the following unexplained symptoms:

- Cough
- Fatigue
- Shortness of breath
- Chest pain
- Weight loss
- Appetite loss [new 2015]

Consider an urgent chest X-ray (to be performed within 2 weeks) to assess for lung cancer in people aged 40 and over with any of the following:

- Persistent or recurrent chest infection
- Finger clubbing
- Supraclavicular lymphadenopathy or persistent cervical lymphadenopathy
- Chest signs consistent with lung cancer
- Thrombocytosis [new 2015]

Mesothelioma

Refer people using a suspected cancer pathway referral (for an appointment within 2 weeks) for mesothelioma if they have chest X-ray findings that suggest mesothelioma. [new 2015]

Offer an urgent chest X-ray (to be performed within 2 weeks) to assess for mesothelioma in people aged 40 and over, if:

- They have 2 or more of the following unexplained symptoms, or
- They have 1 or more of the following unexplained symptoms and have ever smoked, or
- They have 1 or more of the following unexplained symptoms and have been exposed to asbestos:
    - Cough
    - Fatigue
    - Shortness of breath
    - Chest pain
    - Weight loss
    - Appetite loss [new 2015]

Consider an urgent chest X-ray (to be performed within 2 weeks) to assess for mesothelioma in people aged 40 and over with either:

- Finger clubbing or
- Chest signs compatible with pleural disease [new 2015]

Upper Gastrointestinal Tract Cancers

Oesophageal Cancer

Offer urgent direct access upper gastrointestinal endoscopy (to be performed within 2 weeks) to assess for oesophageal cancer in people:

- With dysphagia or
- Aged 55 and over with weight loss and any of the following:
  - Upper abdominal pain
  - Reflux
  - Dyspepsia [new 2015]

Consider non-urgent direct access upper gastrointestinal endoscopy to assess for oesophageal cancer in people with haematemesis. [new 2015]

Consider non-urgent direct access upper gastrointestinal endoscopy to assess for oesophageal cancer in people aged 55 or over with:

- Treatment-resistant dyspepsia or
- Upper abdominal pain with low haemoglobin levels or
- Raised platelet count with any of the following:
  - Nausea
  - Vomiting
  - Weight loss
  - Reflux
  - Dyspepsia
  - Upper abdominal pain, or
- Nausea or vomiting with any of the following:
  - Weight loss
  - Reflux
  - Dyspepsia
  - Upper abdominal pain [new 2015]

Pancreatic Cancer

Refer people using a suspected cancer pathway referral (for an appointment within 2 weeks) for pancreatic cancer if they are aged 40 and over and have jaundice. [new 2015]

Consider an urgent direct access computed tomography (CT) scan (to be performed within 2 weeks), or an urgent ultrasound scan if CT is not available, to assess for pancreatic cancer in people aged 60 and over with weight loss and any of the following:

- Diarrhoea
- Back pain
- Abdominal pain
- Nausea
- Vomiting
- Constipation
- New-onset diabetes [new 2015]

Stomach Cancer

Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for people with an upper abdominal mass consistent with stomach cancer. [new 2015]

Offer urgent direct access upper gastrointestinal endoscopy (to be performed within 2 weeks) to assess for stomach cancer in people:

- With dysphagia or
- Aged 55 and over with weight loss and any of the following:
  - Upper abdominal pain
  - Reflux
  - Dyspepsia [new 2015]

Consider non-urgent direct access upper gastrointestinal endoscopy to assess for stomach cancer in people with haematemesis. [new 2015]

Consider non-urgent direct access upper gastrointestinal endoscopy to assess for stomach cancer in people aged 55 or over with:

- Treatment-resistant dyspepsia or
- Upper abdominal pain with low haemoglobin levels or
- Raised platelet count with any of the following:
    - Nausea
    - Vomiting
    - Weight loss
    - Reflux
    - Dyspepsia
    - Upper abdominal pain, or
- Nausea or vomiting with any of the following:
    - Weight loss
    - Reflux
    - Dyspepsia
    - Upper abdominal pain [new 2015]

Gall Bladder Cancer

Consider an urgent direct access ultrasound scan (to be performed within 2 weeks) to assess for gall bladder cancer in people with an upper abdominal mass consistent with an enlarged gall bladder. [new 2015]

Liver Cancer

Consider an urgent direct access ultrasound scan (to be performed within 2 weeks) to assess for liver cancer in people with an upper abdominal mass consistent with an enlarged liver. [new 2015]

Lower Gastrointestinal Tract Cancers

Colorectal Cancer

Refer people using a suspected cancer pathway referral (for an appointment within 2 weeks) for colorectal cancer if:

- They are aged 40 and over with unexplained weight loss and abdominal pain or
- They are aged 50 and over with unexplained rectal bleeding or
- They are aged 60 and over with:
    - Iron-deficiency anaemia or
    - Changes in their bowel habit, or
- Tests show occult blood in their faeces (see recommendation below for who should be offered a test for occult blood in faeces). [new 2015]

Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for colorectal cancer in people with a rectal or abdominal mass. [new 2015]

Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for colorectal cancer in adults aged under 50 with rectal bleeding and any of the following unexplained symptoms or findings:

- Abdominal pain
- Change in bowel habit
- Weight loss
- Iron-deficiency anaemia [new 2015]

Offer testing for occult blood in faeces to assess for colorectal cancer in adults without rectal bleeding who:

- Are aged 50 and over with unexplained:
    - Abdominal pain or
    - Weight loss, or
- Are aged under 60 with:
    - Changes in their bowel habit or
    - Iron-deficiency anaemia, or
- Are aged 60 and over and have anaemia even in the absence of iron deficiency [new 2015]

Anal Cancer

Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for anal cancer in people with an unexplained anal mass or unexplained anal ulceration. [new 2015]

Breast Cancer

Refer people using a suspected cancer pathway referral (for an appointment within 2 weeks) for breast cancer if they are:

- Aged 30 and over and have an unexplained breast lump with or without pain or
- Aged 50 and over with any of the following symptoms in one nipple only:
  - Discharge
  - Retraction
  - Other changes of concern [new 2015]

Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for breast cancer in people:

- With skin changes that suggest breast cancer or
- Aged 30 and over with an unexplained lump in the axilla [new 2015]

Consider non-urgent referral in people aged under 30 with an unexplained breast lump with or without pain. See also "Recommendations on Patient Support, Safety Netting and the Diagnostic Process" below for information about seeking specialist advice. [new 2015]

Gynaecological Cancers

Ovarian Cancer

The recommendations in this section have been incorporated from NICE clinical guideline on ovarian cancer (NICE guideline CG122) (see Ovarian cancer. The recognition and initial management of ovarian cancer) and have not been updated. The recommendations for ovarian cancer apply to women aged 18 and over.

Refer the woman urgently[1] if physical examination identifies ascites and/or a pelvic or abdominal mass (which is not obviously uterine fibroids). [2011]

Carry out tests in primary care (see recommendations below) if a woman (especially if 50 or over) reports having any of the following symptoms on a persistent or frequent basis – particularly more than 12 times per month:

- Persistent abdominal distension (women often refer to this as 'bloating')
- Feeling full (early satiety) and/or loss of appetite
- Pelvic or abdominal pain
- Increased urinary urgency and/or frequency [2011]

Consider carrying out tests in primary care (see recommendations below) if a woman reports unexplained weight loss, fatigue or changes in bowel habit. [2011]

Advise any woman who is not suspected of having ovarian cancer to return to her general practitioner (GP) if her symptoms become more frequent and/or persistent. [2011]

Carry out appropriate tests for ovarian cancer (see recommendations below) in any woman of 50 or over who has experienced symptoms within the last 12 months that suggest irritable bowel syndrome (IBS)[2], because IBS rarely presents for the first time in women of this age. [2011]

Measure serum CA125 in primary care in women with symptoms that suggest ovarian cancer (see recommendations above). [2011]

If serum CA125 is 35 IU/ml or greater, arrange an ultrasound scan of the abdomen and pelvis. [2011]

If the ultrasound suggests ovarian cancer, refer the woman urgently[1] for further investigation. [2011]

For any woman who has normal serum CA125 (less than 35 IU/ml), or CA125 of 35 IU/ml or greater but a normal ultrasound:

- Assess her carefully for other clinical causes of her symptoms and investigate if appropriate
- If no other clinical cause is apparent, advise her to return to her GP if her symptoms become more frequent and/or persistent [2011]

[1]An urgent referral means that the woman is referred to a gynaecological cancer service within the national target in England and Wales for referral for suspected cancer, which is currently 2 weeks.

[2]See the NICE guideline on Irritable bowel syndrome in adults .

Endometrial Cancer

Refer women using a suspected cancer pathway referral (for an appointment within 2 weeks) for endometrial cancer if they are aged 55 and over with post-menopausal bleeding (unexplained vaginal bleeding more than 12 months after menstruation has stopped because of the menopause). [new 2015]

Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for endometrial cancer in women aged under 55 with post-menopausal bleeding. [new 2015]

Consider a direct access ultrasound scan to assess for endometrial cancer in women aged 55 and over with:

- Unexplained symptoms of vaginal discharge who:
    - Are presenting with these symptoms for the first time or
    - Have thrombocytosis or
    - Report haematuria, or
- Visible haematuria and:
    - Low haemoglobin levels or
    - Thrombocytosis or
    - High blood glucose levels [new 2015]

Cervical Cancer

Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for women if, on examination, the appearance of their cervix is consistent with cervical cancer. [new 2015]

Vulval Cancer

Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for vulval cancer in women with an unexplained vulval lump, ulceration or bleeding. [new 2015]

Vaginal Cancer

Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for vaginal cancer in women with an unexplained palpable mass in or at the entrance to the vagina. [new 2015]

Urological Cancers

Prostate Cancer

Refer men using a suspected cancer pathway referral (for an appointment within 2 weeks) for prostate cancer if their prostate feels malignant on digital rectal examination. [new 2015]

Consider a prostate-specific antigen (PSA) test and digital rectal examination to assess for prostate cancer in men with:

- Any lower urinary tract symptoms, such as nocturia, urinary frequency, hesitancy, urgency or retention or
- Erectile dysfunction or
- Visible haematuria [new 2015]

Refer men using a suspected cancer pathway referral (for an appointment within 2 weeks) for prostate cancer if their PSA levels are above the age-specific reference range. [new 2015]

Bladder Cancer

Refer people using a suspected cancer pathway referral (for an appointment within 2 weeks) for bladder cancer if they are:

- Aged 45 and over and have:
    - Unexplained visible haematuria without urinary tract infection or

- Visible haematuria that persists or recurs after successful treatment of urinary tract infection, or
- Aged 60 and over and have unexplained non-visible haematuria and either dysuria or a raised white cell count on a blood test [new 2015]

Consider non-urgent referral for bladder cancer in people aged 60 and over with recurrent or persistent unexplained urinary tract infection. [new 2015]

Renal Cancer

Refer people using a suspected cancer pathway referral (for an appointment within 2 weeks) for renal cancer if they are aged 45 and over and have:

- Unexplained visible haematuria without urinary tract infection or
- Visible haematuria that persists or recurs after successful treatment of urinary tract infection [new 2015]

Testicular Cancer

Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for testicular cancer in men if they have a non-painful enlargement or change in shape or texture of the testis. [new 2015]

Consider a direct access ultrasound scan for testicular cancer in men with unexplained or persistent testicular symptoms. [new 2015]

Penile Cancer

Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for penile cancer in men if they have either:

- A penile mass or ulcerated lesion, where a sexually transmitted infection has been excluded as a cause, or
- A persistent penile lesion after treatment for a sexually transmitted infection has been completed [new 2015]

Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for penile cancer in men with unexplained or persistent symptoms affecting the foreskin or glans. [new 2015]

Skin Cancers

Malignant Melanoma of the Skin

Refer people using a suspected cancer pathway referral (for an appointment within 2 weeks) for melanoma if they have a suspicious pigmented skin lesion with a weighted 7-point checklist score of 3 or more. [new 2015]

Weighted 7-Point Checklist

Major features of the lesions (scoring 2 points each):

- Change in size
- Irregular shape
- Irregular colour

Minor features of the lesions (scoring 1 point each):

- Largest diameter 7 mm or more
- Inflammation
- Oozing
- Change in sensation

Refer people using a suspected cancer pathway referral (for an appointment within 2 weeks) if dermoscopy suggests melanoma of the skin. [new 2015]

Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for melanoma in people with a pigmented or non-pigmented skin lesion that suggests nodular melanoma. [new 2015]

Squamous Cell Carcinoma

Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for people with a skin lesion that raises the suspicion of squamous cell carcinoma. [new 2015]

Basal Cell Carcinoma

Consider routine referral for people if they have a skin lesion that raises the suspicion of a basal cell carcinoma[3]. [new 2015]

Only consider a suspected cancer pathway referral (for an appointment within 2 weeks) for people with a skin lesion that raises the suspicion of a basal cell carcinoma if there is particular concern that a delay may have a significant impact, because of factors such as lesion site or size. [new 2015]

Follow the NICE guidance on Improving outcomes for people with skin tumours including melanoma: the management of low-risk basal cell carcinomas in the community (2010 update) for advice on who should excise suspected basal cell carcinomas. [new 2015]

[3]Typical features of basal cell carcinoma include: an ulcer with a raised rolled edge; prominent fine blood vessels around a lesion; or a nodule on the skin (particularly pearly or waxy nodules).

Head and Neck Cancers

Laryngeal Cancer

Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for laryngeal cancer in people aged 45 and over with:

- Persistent unexplained hoarseness or
- An unexplained lump in the neck [new 2015]

Oral Cancer

Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for oral cancer in people with either:

- Unexplained ulceration in the oral cavity lasting for more than 3 weeks or
- A persistent and unexplained lump in the neck [new 2015]

Consider an urgent referral (for an appointment within 2 weeks) for assessment for possible oral cancer by a dentist in people who have either:

- A lump on the lip or in the oral cavity or
- A red or red and white patch in the oral cavity consistent with erythroplakia or erythroleukoplakia [new 2015]

Consider a suspected cancer pathway referral by the dentist (for an appointment within 2 weeks) for oral cancer in people when assessed by a dentist as having either:

- A lump on the lip or in the oral cavity consistent with oral cancer or
- A red or red and white patch in the oral cavity consistent with erythroplakia or erythroleukoplakia [new 2015]

Thyroid Cancer

Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for thyroid cancer in people with an unexplained thyroid lump. [new 2015]

Brain and Central Nervous System Cancers

Adults

Consider an urgent direct access magnetic resonance imaging (MRI) scan of the brain (or CT scan if MRI is contraindicated) (to be performed within 2 weeks) to assess for brain or central nervous system cancer in adults with progressive, sub-acute loss of central neurological function. [new 2015]

Children and Young People

Consider a very urgent referral (for an appointment within 48 hours) for suspected brain or central nervous system cancer in children and young people with newly abnormal cerebellar or other central neurological function. [new 2015]

Haematological Cancers

Leukaemia in Adults

Consider a very urgent full blood count (within 48 hours) to assess for leukaemia in adults with any of the following:

- Pallor
- Persistent fatigue
- Unexplained fever
- Unexplained persistent or recurrent infection
- Generalised lymphadenopathy
- Unexplained bruising
- Unexplained bleeding
- Unexplained petechiae
- Hepatosplenomegaly [new 2015]

Leukaemia in Children and Young People

Refer children and young people for immediate specialist assessment for leukaemia if they have unexplained petechiae or hepatosplenomegaly. [new 2015]

Offer a very urgent full blood count (within 48 hours) to assess for leukaemia in children and young people with any of the following:

- Pallor
- Persistent fatigue
- Unexplained fever
- Unexplained persistent infection
- Generalised lymphadenopathy
- Persistent or unexplained bone pain
- Unexplained bruising
- Unexplained bleeding [new 2015]

Myeloma

Offer a full blood count, blood tests for calcium and plasma viscosity or erythrocyte sedimentation rate to assess for myeloma in people aged 60 and over with persistent bone pain, particularly back pain, or unexplained fracture. [new 2015]

Offer very urgent protein electrophoresis and a Bence-Jones protein urine test (within 48 hours) to assess for myeloma in people aged 60 and over with hypercalcaemia or leukopenia and a presentation that is consistent with possible myeloma. [new 2015]

Consider very urgent protein electrophoresis and a Bence-Jones protein urine test (within 48 hours) to assess for myeloma if the plasma viscosity or erythrocyte sedimentation rate and presentation are consistent with possible myeloma. [new 2015]

Refer people using a suspected cancer pathway referral (for an appointment within 2 weeks) if the results of protein electrophoresis or a Bence-Jones protein urine test suggest myeloma. [new 2015]

Non-Hodgkin's Lymphoma in Adults

Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for non-Hodgkin's lymphoma in adults[4] presenting with unexplained lymphadenopathy or splenomegaly. When considering referral, take into account any associated symptoms, particularly fever, night sweats, shortness of breath, pruritus or weight loss. [new 2015]

Non-Hodgkin's Lymphoma in Children and Young People

Consider a very urgent referral (for an appointment within 48 hours) for specialist assessment for non-Hodgkin's lymphoma in children and young people[4] presenting with unexplained lymphadenopathy or splenomegaly. When considering referral, take into account any associated symptoms, particularly fever, night sweats, shortness of breath, pruritus or weight loss. [new 2015]

Hodgkin's Lymphoma in Adults

Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for Hodgkin's lymphoma in adults[4] presenting with unexplained lymphadenopathy. When considering referral, take into account any associated symptoms, particularly fever, night sweats, shortness of breath, pruritus, weight loss or alcohol-induced lymph node pain. [new 2015]

Hodgkin's Lymphoma in Children and Young People

Consider a very urgent referral (for an appointment within 48 hours) for specialist assessment for Hodgkin's lymphoma in children and young people[4] presenting with unexplained lymphadenopathy. When considering referral, take into account any associated symptoms, particularly fever, night sweats, shortness of breath, pruritus or weight loss. [new 2015]

Sarcomas

Bone Sarcoma in Adults

Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for adults[4] if an X-ray suggests the possibility of bone sarcoma. [new 2015]

Bone Sarcoma in Children and Young People

Consider a very urgent referral (for an appointment within 48 hours) for specialist assessment for children and young people[4] if an X-ray suggests the possibility of bone sarcoma. [new 2015]

Consider a very urgent direct access X-ray (to be performed within 48 hours) to assess for bone sarcoma in children and young people with unexplained bone swelling or pain. [new 2015]

Soft Tissue Sarcoma in Adults

Consider an urgent direct access ultrasound scan (to be performed within 2 weeks) to assess for soft tissue sarcoma in adults[4] with an unexplained lump that is increasing in size. [new 2015]

Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for adults[4] if they have ultrasound scan findings that are suggestive of soft tissue sarcoma or if ultrasound findings are uncertain and clinical concern persists. [new 2015]

Soft Tissue Sarcoma in Children and Young People

Consider a very urgent direct access ultrasound scan (to be performed within 48 hours) to assess for soft tissue sarcoma in children and young people[4] with an unexplained lump that is increasing in size. [new 2015]

Consider a very urgent referral (for an appointment within 48 hours) for children and young people[4] if they have ultrasound scan findings that are suggestive of soft tissue sarcoma or if ultrasound findings are uncertain and clinical concern persists. [new 2015]

[4]Separate recommendations have been made for adults and for children and young people to reflect that there are different referral pathways. However, in practice young people (aged 16–24) may be referred using either an adult or children's pathway depending on their age and local arrangements.

Childhood Cancers

Neuroblastoma

Consider very urgent referral (for an appointment within 48 hours) for specialist assessment for neuroblastoma in children with a palpable abdominal mass or unexplained enlarged abdominal organ. [new 2015]

Retinoblastoma

Consider urgent referral (for an appointment within 2 weeks) for ophthalmological assessment for retinoblastoma in children with an absent red reflex. [new 2015]

Wilms' Tumour

Consider very urgent referral (for an appointment within 48 hours) for specialist assessment for Wilms' tumour in children with any of the following:

- A palpable abdominal mass
- An unexplained enlarged abdominal organ

- Unexplained visible haematuria [new 2015]

Non-Site-Specific Symptoms

Some symptoms or symptom combinations may be features of several different cancers. For some of these symptoms, the risk for each individual cancer may be low but the total risk of cancer of any type may be higher. This section includes recommendations for these symptoms.

Symptoms of Concern in Children and Young People

Take into account the insight and knowledge of parents and carers when considering making a referral for suspected cancer in a child or young person. Consider referral for children if their parent or carer has persistent concern or anxiety about the child's symptoms, even if the symptoms are most likely to have a benign cause. [2015]

Symptoms of Concern in Adults

For people with unexplained weight loss, which is a symptom of several cancers including colorectal, gastro-oesophageal, lung, prostate, pancreatic and urological cancer:

- Carry out an assessment for additional symptoms, signs or findings that may help to clarify which cancer is most likely and
- Offer urgent investigation or a suspected cancer pathway referral (for an appointment within 2 weeks) [new 2015]

For people with unexplained appetite loss, which is a symptom of several cancers including lung, oesophageal, stomach, colorectal, pancreatic, bladder and renal cancer:

- Carry out an assessment for additional symptoms, signs or findings that may help to clarify which cancer is most likely and
- Offer urgent investigation or a suspected cancer pathway referral (for an appointment within 2 weeks) [new 2015]

For people with deep vein thrombosis, which is associated with several cancers including urogenital, breast, colorectal and lung cancer:

- Carry out an assessment for additional symptoms, signs or findings that may help to clarify which cancer is most likely and
- consider urgent investigation or a suspected cancer pathway referral (for an appointment within 2 weeks) [new 2015]

Recommendations on Patient Support, Safety Netting and the Diagnostic Process

Patient Information and Support

Discuss with people with suspected cancer (and their carers as appropriate, taking account of the need for confidentiality) their preferences for being involved in decision-making about referral options and further investigations including their potential risks and benefits. [2015]

When cancer is suspected in a child, discuss the referral decision and information to be given to the child with the parents or carers (and the child if appropriate). [2015]

Explain to people who are being referred with suspected cancer that they are being referred to a cancer service. Reassure them, as appropriate, that most people referred will not have a diagnosis of cancer, and discuss alternative diagnoses with them. [2015]

Give the person information on the possible diagnosis (both benign and malignant) in accordance with their wishes for information (see also the NICE guideline on Patient experience in adult NHS services). [2015]

The information given to people with suspected cancer and their families and/or carers should cover, among other issues:

- Where the person is being referred to
- How long they will have to wait for the appointment
- How to obtain further information about the type of cancer suspected or help before the specialist appointment
- What to expect from the service the person will be attending
- What type of tests may be carried out, and what will happen during diagnostic procedures
- How long it will take to get a diagnosis or test results
- Whether they can take someone with them to the appointment
- Who to contact if they do not receive confirmation of an appointment
- other sources of support [new 2015]

Provide information that is appropriate for the person in terms of language, ability and culture, recognising the potential for different cultural

meanings associated with the possibility of cancer. [2015]

Have information available in a variety of formats on both local and national sources of information and support for people who are being referred with suspected cancer. For more information on information sharing, see section 1.5 in the NICE guideline on Patient experience in adult NHS services . [new 2015]

Reassure people in the safety netting group (see recommendation below) who are concerned that they may have cancer that with their current symptoms their risk of having cancer is low. [new 2015]

Explain to people who are being offered safety netting (see recommendation below) which symptoms to look out for and when they should return for re-evaluation. It may be appropriate to provide written information. [new 2015]

When referring a person with suspected cancer to a specialist service, assess their need for continuing support while waiting for their referral appointment. This should include inviting the person to contact their healthcare professional again if they have more concerns or questions before they see a specialist. [2005]

If the person has additional support needs because of their personal circumstances, inform the specialist (with the person's agreement). [2005]

Safety Netting

Ensure that the results of investigations are reviewed and acted upon appropriately, with the healthcare professional who ordered the investigation taking or explicitly passing on responsibility for this. Be aware of the possibility of false-negative results for chest X-rays and tests for occult blood in faeces. [new 2015]

Consider a review for people with any symptom that is associated with an increased risk of cancer, but who do not meet the criteria for referral or other investigative action. The review may be:

- Planned within a time frame agreed with the person or
- Patient-initiated if new symptoms develop, the person continues to be concerned, or their symptoms recur, persist or worsen [new 2015]

The Diagnostic Process

Take part in continuing education, peer review and other activities to improve and maintain clinical consulting, reasoning and diagnostic skills, in order to identify at an early stage people who may have cancer, and to communicate the possibility of cancer to the person. [2005]

Discussion with a specialist (for example, by telephone or email) should be considered if there is uncertainty about the interpretation of symptoms and signs, and whether a referral is needed. This may also enable the primary healthcare professional to communicate their concerns and a sense of urgency to secondary healthcare professionals when symptoms are not classical. [2005]

Put in place local arrangements to ensure that letters about non-urgent referrals are assessed by the specialist, so that the person can be seen more urgently if necessary. [2005]

Put in place local arrangements to ensure that there is a maximum waiting period for non-urgent referrals, in accordance with national targets and local arrangements. [2005]

Ensure local arrangements are in place to identify people who miss their appointments so that they can be followed up. [2005]

Include all appropriate information in referral correspondence, including whether the referral is urgent or non-urgent. [2005]

Use local referral proformas if these are in use. [2005]

Once the decision to refer has been made, make sure that the referral is made within 1 working day. [2005]

Refer to the original guideline document for recommendations organised by symptom and findings of primary care investigations.

Definitions

Strength of Recommendations

Some recommendations can be made with more certainty than others. The Guideline Development Group (GDG) makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the GDG is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in

the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

Interventions That Must (or Must Not) Be Used

The GDG usually uses 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally the GDG uses 'must' (or 'must not') if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

Interventions That Should (or Should Not) Be Used – a 'Strong' Recommendation

The GDG uses 'offer' (and similar words such as 'refer' or 'advise') when confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective. The GDG uses similar forms of words (for example, 'Do not offer…') when confident that an intervention will not be of benefit for most patients.

Interventions That Could Be Used

The GDG uses 'consider' when the GDG is confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

Recommendation Wording in Guideline Updates

NICE began using this approach to denote the strength of recommendations in guidelines that started development after publication of the 2009 version of 'The guidelines manual' (January 2009). This does not apply to any recommendations ending [2005]. In particular, for recommendations labelled [2005], the word 'consider' may not necessarily be used to denote the strength of the recommendation.

Clinical Algorithm(s)

The following National Institute for Health and Care Excellence (NICE) pathways are provided on the NICE Web site :

- Lung cancer
- Suspected cancer recognition and referral

Scope

Disease/Condition(s)

Suspected cancer including:

- Lung and pleural cancers
- Upper gastrointestinal tract cancers
- Lower gastrointestinal tract cancers
- Breast cancer
- Gynaecological cancers
- Urological cancers
- Skin cancers
- Head and neck cancers
- Brain and central nervous system cancers
- Haematological cancers
- Sarcomas
- Childhood cancers

Guideline Category

Diagnosis

Evaluation

Risk Assessment

Clinical Specialty

Dentistry

Family Practice

Internal Medicine

Obstetrics and Gynecology

Oncology

Pediatrics

Intended Users

Advanced Practice Nurses

Dentists

Health Care Providers

Optometrists

Patients

Physician Assistants

Physicians

Guideline Objective(s)

- To provide recommendations on recognition and selection for referral or investigation in primary care of people of all ages, including children and young people, who may have cancer
- To offer best practice advice on the care of people with suspected cancer
- To help people understand what to expect if they have symptoms that may suggest cancer
- To help those in secondary care to understand which services should be provided for people with suspected cancer

Target Population

Patients in all age groups suspected of having one of the cancers covered by the guideline

Note: Although the terms 'men' and 'women' are used for recommendations on gender-related cancers, these recommendations also extend to people who have changed or are in the process of changing gender, and who retain the relevant organs.

Interventions and Practices Considered

1. Initial investigations for assessment of patients prior to, or in association with, referral for suspected cancer, where clinical responsibility is retained by primary care
2. Immediate referral to secondary care using the existing 2-week referral system
3. Consideration of signs and symptoms that indicate the possibility of a cancer diagnosis
4. Consideration of abnormal blood test results that indicate the possibility of a cancer diagnosis
5. Providing for the information needs of patients who are referred for suspected cancer and for patients who are being monitored in primary

care, as well as their family and carers
6. Follow-up plans (including 'safety-netting') for patients whose care is managed in primary care without referral for definitive investigation
7. Special considerations for children and young people

Major Outcomes Considered

- Health-related quality of life
- Sensitivity of symptoms/signs and diagnostic tests
- Specificity of symptoms/signs and diagnostic tests
- Positive predictive value of symptoms/signs and diagnostic tests
- Negative predictive value of symptoms/signs and diagnostic tests
- Cost-effectiveness

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Cancer (NCC-C) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

From each of the key clinical issues identified in the scope, the Guideline Development Group (GDG) formulated a clinical question. For the clinical questions, the PICO framework was used. This structured approach divides each question into four components: P – the population (the population under study), I – the index test, or sign/symptom (what is being done; for the signs and symptoms questions, a patient presenting with a sign/symptom was considered to be test positive), C – the comparison (other main test options; in this case the reference standard), O – the outcomes (the measures of how effective the tests have been).

Review of Clinical Literature

Scoping Search

An initial scoping search for published guidelines, systematic reviews, economic evaluations and ongoing research was carried out on the following databases or websites: National Health Service (NHS) Evidence, Cochrane Databases of Systematic Reviews (CDSR), Health Technology Assessment Database (HTA), NHS Economic Evaluations Database (NHS EED), Health Economic Evaluations Database (HEED), Medline and EMBASE.

At the beginning of the development phase, initial scoping searches were carried out to identify any relevant guidelines (local, national or international) produced by other groups or institutions.

Developing the Review Protocol

For each clinical question, the information specialist and researcher (with input from other technical team and GDG members) prepared a review protocol. This protocol explains how the review was to be carried out in order to develop a plan of how to review the evidence, limit the introduction of bias and for the purposes of reproducibility. All review protocols can be found in the evidence review.

Searching for the Evidence

In order to answer each question the NCC-C information specialist developed a search strategy to identify relevant published evidence for both clinical and cost-effectiveness. Key words and terms for the search were agreed in collaboration with the GDG. When required, the health economist searched for supplementary papers to inform detailed health economic work (see "Incorporating Health Economic Evidence" below).

A specific filter was developed by the NCC-C to identify only primary care based studies, as people with symptoms in primary care were the population of relevance to this guideline. Prior to use, the accuracy of this filter was tested by using it to run searches for symptoms of colorectal cancer (a common cancer) and for symptoms of bladder cancer (a less common cancer). The results of these searches were then compared against the list of papers included in two published systematic reviews of symptoms of bladder and colorectal cancer in primary care. All of the papers in the systematic reviews, except one per review, were identified by the searches run with the primary care filter. The two papers that were not identified by the searches using the primary care filter were investigated further and it was established that they had not been found due to issues with the indexing of the paper. This information was presented to the GDG during a GDG meeting and they agreed that the primary care filter was accurate and appropriate for use.

No language restrictions were applied to the search.

The following databases were included in the literature search:

- The Cochrane Library
- Medline and Premedline 1946 onwards
- Excerpta Medica (EMBASE) 1974 onwards
- Web of Science (all databases 1899 onwards)

Subject specific databases used for certain topics:

- Cumulative Index to Nursing and Allied Health Literature (CINAHL) 1937 onwards
- Allied & Complementary Medicine (AMED) 1985 onwards
- PsycINFO 1806 onwards

From this list the information specialist sifted and removed any irrelevant material based on the title or abstract before passing to the researcher. All the remaining articles were then stored in a Reference Manager electronic library.

The evidence was searched by cancer site because symptoms may represent several different cancers; furthermore, symptoms are often not included in the title or abstract of research outputs, so relevant publications could have been lost from the searches if the GDG had searched by symptom alone.

Searches were updated and re-run 8 to 10 weeks before the stakeholder consultation, thereby ensuring that the latest relevant published evidence was included in the database. Any evidence published after this date was not included. For the purposes of updating this guideline, August 2014 should be considered the starting point for searching for new evidence.

Further details of the search strategies, including the methodological filters used, are provided in the evidence review in Appendix F in the full guideline appendices (see the "Availability of Companion Documents" field).

Critical Appraisal and Evidence Grading

Following the literature search one researcher independently scanned the titles and abstracts of every article for each question, and full publications were obtained for any studies considered relevant or where there was insufficient information from the title and abstract to make a decision. When papers were obtained, the researcher applied inclusion/exclusion criteria to select appropriate studies, which were then critically appraised.

Incorporating Health Economics Evidence

Prioritising Topics for Economic Analysis

After the clinical questions had been defined, and with the help of the health economist, the GDG discussed and agreed which of the clinical questions were potential priorities for economic analysis. These economic priorities were chosen on the basis of the following criteria, in broad accordance with the NICE guidelines manual (NICE 2012) (see the "Availability of Companion Documents" field):

- The overall importance of the recommendation, which may be a function of the number of patients affected and the potential impact on costs and health outcomes per patient
- The current extent of uncertainty over cost effectiveness, and the likelihood that economic analysis will reduce this uncertainty
- The feasibility of building an economic model

A review of the economic literature was conducted at scoping. Where published economic evaluation studies were identified that addressed the economic issues for a clinical question, these are presented alongside the clinical evidence. For those clinical areas reviewed, the information specialists used a similar search strategy as used for the review of clinical evidence but with the inclusion of a health economics filter instead of the primary care filter.

For systematic searches of published economic evidence, the following databases were included:

- Medline
- EMBASE
- NHS EED
- HTA
- HEED

Number of Source Documents

See the "Clinical Evidence" sections for each type of cancer and Appendix F in the full guideline appendices (see the "Availability of Companion Documents" field) for details regarding the number and type of included studies.

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Weighting According to a Rating Scheme (Scheme Not Given)

Rating Scheme for the Strength of the Evidence

The quality of individual diagnostic accuracy studies was assessed using the Quality Assessment of Studies of Diagnostic Accuracy (QUADAS)-2 tool. A modified version of this tool (including three extra items specifically aimed at diagnostic case-control studies) was used to assess the quality of the evidence for the questions about signs and symptoms of the individual cancers. The QUADAS-2 tool is not designed to provide an overall quality of the evidence, but was used to identify potentially important areas where there was a high risk of bias or high concerns about applicability of the evidence, which in turn, were used to inform the overall estimates of the evidence quality in the Linking Evidence to Recommendations (LETR) sections. The same reviewer rated the overall quality of the evidence for all the clinical questions with input from the Guideline Development Group (GDG). The aim of these ratings was to be as consistent as possible, but without them being too specific when that was clearly not possible (for example by using "not high" when not able to clearly make an overall rating of moderate, low or very low).

Methods Used to Analyze the Evidence

Meta-Analysis

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Cancer (NCC-C) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Review of Clinical Literature

Critical Appraisal and Evidence Grading

For each question, data were extracted and recorded in evidence tables and an accompanying evidence summary prepared for the Guideline

Development Group (GDG). All evidence was considered carefully by the GDG for accuracy and completeness.

For non-interventional questions, for example the questions regarding diagnostic test accuracy, a narrative summary of the quality of the evidence was provided. The quality of individual diagnostic accuracy studies was assessed using the Quality Assessment of Studies of Diagnostic Accuracy (QUADAS)-2 tool. A modified version of this tool (including three extra items specifically aimed at diagnostic case-control studies) was used to assess the quality of the evidence for the questions about signs and symptoms of the individual cancers. The QUADAS-2 tool is not designed to provide an overall quality of the evidence, but was used to identify potentially important areas where there was a high risk of bias or high concerns about applicability of the evidence, which in turn, were used to inform the overall estimates of the evidence quality in the Linking Evidence to Recommendations (LETR) sections. The same reviewer rated the overall quality of the evidence for all the clinical questions with input from the GDG. The aim of these ratings was to be as consistent as possible, but without them being too specific when that was clearly not possible (for example by using "not high" when not able to clearly make an overall rating of moderate, low or very low). The specific issues with the evidence are detailed in the QUADAS-2 figures and "Risk of Bias in the Included Studies" sections and in the evidence section. Grading of Recommendations Assessment, Development and Evaluation (GRADE) was not used for the overall evidence quality ratings because it was still under development for diagnostic studies at the start of this guideline.

Meta-analysis was undertaken when it was feasible to do so, i.e., when there were at least three studies with study populations and symptoms that were considered similar enough to combine. Case-control studies were never included in these meta-analyses due to the different nature of the data, compared to the studies employing consecutive patient series. A minimum of three studies were required to perform the meta-analysis due to the need for a minimum number of data points relative to the number of parameters that were estimated during the analysis. In cases where sufficient data were available, secondary analyses were performed that excluded papers with particular quality or applicability concerns. Although reviewers sought to perform meta-analyses for different age groups/genders, the data were never available for consistent age groups, or the two genders, in a sufficient number of studies for the same symptoms. This meant that the meta-analyses received less weight by the GDG than the individual studies that provided positive predictive values split by age and gender because age is such an important risk factor of cancer.

In addition to positive predictive values (PPVs), the incidence of symptoms observed in cases and controls were sometimes reported in the results tables for case-control studies. This was because corresponding positive predictive values were not always available for these symptoms but the information was deemed to be potentially relevant to the GDG, especially in cancers where little other evidence was available. However, the GDG tended not to use this additional information when considering the evidence. Confidence intervals were included whenever possible for the reported positive predictive values. The GDG mainly used the point estimates to make decisions about the individual symptoms or symptom combinations, but where they did consider the confidence intervals (usually where the point estimate was above the pre-specified PPV threshold but based on a low number of patients and therefore subject to high levels of uncertainty) this has been explicitly documented in the LETR sections in the full version of the guideline.

At What Value Should the Risk Threshold Be?

Previous guidance used a disparate range of percentage risks of cancer in their recommendations. Few corresponded with a PPV of lower than 5%. The GDG felt that, in order to improve diagnosis of cancer, a PPV threshold lower than 5% was preferable. Patient viewpoints were central to the decision about where the risk threshold should be. The GDG aspired to broaden recommendations to try and improve the timeliness and quality of cancer diagnosis. The lower the threshold could reasonably be set, the more patients with cancer would have expedited diagnoses, with accompanying improvements in mortality and morbidity.

Also germane to the selection of a risk threshold are the resource implications of change. At the time of setting the threshold figure, there were no strong quality health-economic reports which could help with the decision. Many reports could describe the costs involved in expanding cancer diagnostics. The benefits from expedited diagnosis were much less clear. It was, however, clear that broadening of recommendations would bring economic and clinical costs. The clinical costs include potential harms to the patient through the side effects of investigations performed and also through increased anxiety. The lower a threshold is set, the more likely people are to be exposed to these potential harms.

Taking all of this into account, the GDG agreed to use a threshold value of 3% PPV to underpin their recommendations. This value represented a considerable liberalisation of the estimated PPVs of previous recommendations, but the GDG agreed that this change would not overwhelm clinical services, nor greatly increase the possible harms to patients from over-investigation. This 3% PPV governed recommendations for suspected cancer pathway referrals. The GDG considered whether this PPV threshold should be varied in recognition of the fact that some cancers have a poorer prognosis than others. However, for many of the cancers with poorer prognosis, there is neither clinical evidence nor agreement in the wider clinical community that earlier detection would improve prognosis, nor evidence that there are highly effective treatments that could be employed to improve prognosis in individual cases. Given this the GDG agreed to keep the same PPV threshold for suspected cancer pathway referrals in all adult cancers.

The GDG also resolved to apply the same 3% PPV threshold to urgent direct access investigations in secondary care; such as brain scanning or

endoscopy. The exception to this was where it was clear that appropriate investigation using tests previously unavailable to primary care could replace specialist referral. The implied economic advantages of this allowed the GDG to make recommendations below the 3% level. The GDG discussed these on a case by case basis. In instances where patients would not normally be referred on an urgent cancer pathway but would be referred routinely for specialist opinion, the 3% PPV threshold does not apply. The same is true where a non-urgent direct-access test was considered to be more resource efficient.

Two exceptions to the 3% PPV threshold for urgent action were agreed. The first relates to children and young people. As children and young people have longer to live than adults, a successful cancer diagnosis leading to cure should yield more years of life gained. Thus it was agreed that the GDG should make recommendations for children and young people significantly below the 3% PPV threshold, although no explicit threshold value was set.

The second exception relates to tests routinely available in primary care, which can help to refine the underlying risk of cancer - this is the case whether the investigation is being carried out on an urgent basis or otherwise. These include blood tests such as prostate-specific antigen (PSA) or imaging such as chest x-ray.

Symptoms Present in Multiple Cancers but of Low Risk for Each Cancer Site

There are a number of generic symptoms (e.g., fatigue), that, whilst not predictive of a specific cancer, are nevertheless believed to be predictive of 'cancer'. These symptoms will typically be reported by a number of the studies included in the evidence, but will not have high enough PPVs for any individual cancer to meet the threshold for referral or investigation in primary care.

The GDG wanted to examine these symptoms to try to identify those that are predictive of cancer in general, rather than a specific cancer, and make recommendations accordingly.

A spreadsheet was constructed containing all the PPV evidence on the positive predictive values of signs and symptoms for the specific cancers. This spreadsheet was then used as follows:

- Symptoms for which referral recommendations were made for a specific cancer were filtered out of the spreadsheet. This was because these symptoms are predictive of a specific cancer.
- The individual symptoms and symptom combinations were then examined across all the cancer sites where there was evidence for patients across the whole 40-70 age range (this age range was specified in advance by the GDG due to being widely covered in the relevant literature). For each symptom/symptom combination, the highest PPV for each cancer was identified and then added together to create a 'cumulative' PPV. PPVs can be added in this way with the only concern being multiple cancers in the same person. If these were common the 'cumulative' PPVs would be artificially high. However, multiple cancers in the same person at the same time are extremely rare so this issue was judged by the GDG to have negligible impact.

The GDG determined, in advance, that for those symptoms with a 'cumulative' PPV of 2% or above, all the evidence for that symptom across all the cancer sites would be re-examined in detail. The GDG then debated whether recommendations should be made.

The GDG acknowledged that the 'cumulative' PPVs were considered by the GDG to be underestimates. This is due to the likelihood that some cancer site/symptom combinations might not have been reported in the searches, either because the research has not been done, or because the information related to the age range could not be extracted. The GDG therefore chose a threshold of 2% so that they could examine in more detail any instances where the true cumulative PPV might exceed 3% if cancer site/symptom combinations that had not been reported in the literature searches had been available.

Incorporating Health Economics Evidence

Methods for Reviewing and Appraising Economic Evidence

The aim of reviewing and appraising the existing economic literature is to identify relevant economic evaluations that compare both costs and health consequences of alternative interventions and that are applicable to National Health Service (NHS) practice. Thus studies that only report costs, non-comparative studies of 'cost of illness' studies are generally excluded from the reviews.

Economic studies identified through a systematic search of the literature are appraised using a methodology checklist designed for economic evaluations. This checklist is not intended to judge the quality of a study per se, but to determine whether an existing economic evaluation is useful to inform the decision-making of the GDG for a specific topic within the guideline. There are two parts of the appraisal process; the first step is to assess applicability (i.e., the relevance of the study to the specific guideline topic and the NICE reference case).

In the second step, only those studies deemed directly or partially applicable are further assessed for limitations (i.e., the methodological quality).

Where relevant, a summary of the main findings from the systematic search, review and appraisal of economic evidence is presented in an economic evidence profile alongside the clinical evidence.

If high-quality published economic evidence relevant to current NHS practice was identified through the search, the existing literature was reviewed and appraised as described above. However, it is often the case that published economic studies may not be directly relevant to the specific clinical question as defined in the guideline or may not be comprehensive or conclusive enough to inform UK practice. In such cases, for priority topics, consideration was given to undertaking a new economic analysis as part of this guideline.

Economic Modelling

Once the need for a new economic analysis for high priority topics had been agreed by the GDG, the health economist investigated the feasibility of developing an economic model. In the development of the analysis, the following general principles were adhered to:

- The GDG subgroup was consulted during the construction and interpretation of the analysis
- The analysis was based on the best available clinical evidence from the systematic review
- Assumptions were reported fully and transparently
- Uncertainty was explored through sensitivity analysis
- Costs were calculated from a health services perspective
- Outcomes were reported in terms of quality-adjusted life years

Methods Used to Formulate the Recommendations

Expert Consensus

Informal Consensus

Description of Methods Used to Formulate the Recommendations

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Cancer (NCC-C) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

The Guideline Development Group (GDG)

The suspected cancer GDG was recruited in line with the 'NICE guidelines manual' (NICE 2012) (see the "Availability of Companion Documents" field). The first step was to appoint a Chair and a Lead Clinician. Advertisements were placed for both posts and shortlisted candidates were interviewed by telephone prior to being offered the role. The NCC-C Director, GDG Chair and Lead Clinician identified a list of specialties that needed to be represented on the GDG. Details of the adverts were sent to the main stakeholder organisations, cancer networks and patient organisations/charities. Individual GDG members were selected for telephone interview by the NCC-C Director, GDG Chair and Lead Clinician, based on their application forms. The guideline development process was supported by staff from the NCC-C, who undertook the clinical and health economics literature searches, reviewed and presented the evidence to the GDG, managed the process and contributed to drafting the guideline.

GDG Meetings

Seventeen GDG meetings were held between 19-20 June 2012 and 3-4 February 2015. During each GDG meeting (held over either 1 or 2 days) clinical questions and clinical and economic evidence were reviewed, assessed and recommendations formulated. At each meeting patient/carer and service-user concerns were routinely discussed as part of a standing agenda item.

NCC-C project managers divided the GDG workload by allocating specific clinical questions, relevant to their area of clinical practice, to small sub-groups of the GDG in order to simplify and speed up the guideline development process. These groups considered the evidence, as reviewed by the researcher, and synthesised it into draft recommendations before the evidence and draft recommendations were presented to the GDG. These recommendations were then discussed and agreed by the GDG as a whole. Each clinical question was led by a GDG member with expert knowledge of the clinical area (usually one of the healthcare professionals). The GDG subgroups often helped refine the clinical questions and the clinical definitions of treatments. They also assisted the NCC-C team in drafting the section of the guideline relevant to their specific topic.

Patient/Carer Representatives

Individuals with direct experience of suspected cancer services gave an important user focus to the GDG and the guideline development process. The GDG included three patient/carer members. They contributed as full GDG members to writing the clinical questions, helping to ensure that the evidence addressed their views and preferences, highlighting sensitive issues and terminology relevant to the guideline and bringing service-user research to the attention of the GDG.

Expert Advisers

During the development of the guideline the GDG identified two areas (oral cancer and clinical decision support tools) where there was a requirement for expert input. Experts were identified by the NCC-C (see Appendix E in the full guideline appendices [see the "Availability of Companion Documents" field]) and invited to advise the GDG in their consideration of these areas.

Agreeing the Recommendations

For each clinical question the GDG were presented with a summary of the clinical evidence, and, where appropriate, economic evidence, derived from the studies reviewed and appraised. From this information the GDG were able to derive the guideline recommendations. The link between the evidence and the view of the GDG in making each recommendation is made explicitly in the accompanying Linking Evidence to Recommendations (LETR) statement (see below).

LETR Statements

As clinical guidelines were previously formatted, there was limited scope for expressing how and why a GDG made a particular recommendation from the evidence of clinical and cost effectiveness. To make this process more transparent to the reader, NICE has introduced an explicit, easily understood and consistent way of expressing the reasons for making each recommendation. This is known as the 'LETR statement' and will usually cover the following key points:

- The relative value placed on the outcomes considered
- The strength of evidence about benefits and harms for the intervention being considered
- The costs and cost-effectiveness of an intervention
- The quality of the evidence
- The degree of consensus within the GDG
- Other considerations – for example equalities issues

Where evidence was weak or lacking the GDG agreed the final recommendations through informal consensus.

Rating Scheme for the Strength of the Recommendations

Strength of Recommendations

Some recommendations can be made with more certainty than others. The Guideline Development Group (GDG) makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the GDG is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

Interventions That Must (or Must Not) Be Used

The GDG usually uses 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally the GDG uses 'must' (or 'must not') if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

Interventions That Should (or Should Not) Be Used – a 'Strong' Recommendation

The GDG uses 'offer' (and similar words such as 'refer' or 'advise') when confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective. The GDG uses similar forms of words (for example, 'Do not offer…') when confident that an intervention will not be of benefit for most patients.

Interventions That Could Be Used

The GDG uses 'consider' when confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and

discussing the options with the patient.

Recommendation Wording in Guideline Updates

The National Institute for Health and Care Excellence (NICE) began using this approach to denote the strength of recommendations in guidelines that started development after publication of the 2009 version of 'The guidelines manual' (January 2009). This does not apply to any recommendations ending [2005]. In particular, for recommendations labelled [2005], the word 'consider' may not necessarily be used to denote the strength of the recommendation.

Cost Analysis

See details concerning economic evidence for each recommendation in the "Cost-effectiveness evidence" and "Trade-off between net health benefits and resource use" sections of the full version of the guideline (see the "Availability of Companion Documents" field).

See also Appendix A in the full guideline appendices (see the "Availability of Companion Documents" field) for details on the de novo economic model undertaken for this topic.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Involvement of Stakeholders

Key to the development of all National Institute for Health and Care Excellence (NICE) guidelines are the relevant professional and patient/carer organisations that register as stakeholders. Details of this process can be found on the NICE Web site or in the NICE guidelines manual (see the "Availability of Companion Documents" field). In brief, their contribution involves commenting on the draft scope, submitting relevant evidence and commenting on the draft version of the guideline during the end consultation period. A full list of all stakeholder organisations who registered for the suspected cancer guideline can be found in Appendix E in the full guideline appendices (see the "Availability of Companion Documents" field).

Consultation and Validation of the Guideline

The draft of the guideline was prepared by the National Collaborating Centre for Cancer (NCC-C) staff in partnership with the Guideline Development Group (GDG) Chair and Lead Clinician. This was then discussed and agreed with the GDG and subsequently forwarded to NICE for consultation with stakeholders.

Registered stakeholders had one opportunity to comment on the draft guideline which was posted on the NICE Web site between November 20, 2014 and January 9, 2015 in line with NICE methodology.

The Pre-Publication Process

An embargoed pre-publication version of the guideline was released to registered stakeholders to allow them to see how their comments have contributed to the development of the guideline and to give them time to prepare for publication.

The final document was then submitted to NICE for publication on their Web site. The other versions of the guideline were also discussed and approved by the GDG and published at the same time.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is not specifically stated for each recommendation.

The type and quality of evidence supporting each review question are described in evidence profiles in the full version of the guideline (see the "Availability of Companion Documents" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

The Guideline Development Group (GDG) considered that a potential benefit of recommending which symptoms should prompt urgent investigation or referral would be to identify those people with cancer more rapidly. However, the GDG recognised the importance of recommending the 'right' symptoms, in order to minimise the number of people without cancer who get inappropriately referred or assessed whilst maximising the number of people with cancer who get appropriately referred or assessed.

Refer to the "Trade-off between clinical benefits and harms" sections of the full version of the guideline (see the "Availability of Companion Documents" field) for benefits of specific recommendations.

Potential Harms

- Side effects of investigations (e.g., radiation exposure, gastrointestinal bleeding, bowel perforation), increased anxiety
- Inappropriate referrals
- False-positive and false-negative results of cancer diagnostic studies

Refer to the "Trade-off between clinical benefits and harms" sections in the full version of the guideline (see the "Availability of Companion Documents" field) for harms of specific interventions.

Qualifying Statements

Qualifying Statements

- This guidance represents the view of the National Institute for Health and Care Excellence (NICE), which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer, and informed by the summaries of product characteristics of any drugs.
- Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.
- NICE produces guidance, standards and information on commissioning and providing high-quality healthcare, social care, and public health services. NICE has agreements to provide certain NICE services to Wales, Scotland and Northern Ireland. Decisions on how NICE guidance and other products apply in those countries are made by ministers in the Welsh government, Scottish government, and Northern Ireland Executive. NICE guidance or other products may include references to organisations or people responsible for commissioning or providing care that may be relevant only to England.
- See the "Person-centred care" section in the original guideline document for information about individual needs and preferences and transition of care.
- See the original guideline document for information about safeguarding children.

Implementation of the Guideline

Description of Implementation Strategy

Implementation tools and resources to help put the guideline into practice are available (see also the "Availability of Companion Documents" field).

Implementation Tools

Clinical Algorithm

Mobile Device Resources

Patient Resources

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Timeliness

Identifying Information and Availability

Bibliographic Source(s)

National Collaborating Centre for Cancer. Suspected cancer: recognition and referral. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Jun 23. 95 p. (NICE guideline; no. 12).

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2005 Jun (revised 2015 Jun 23)

Guideline Developer(s)

National Guideline Alliance - National Government Agency [Non-U.S.]

Source(s) of Funding

The National Collaborating Centre for Cancer (NCC-C) was commissioned by the National Institute for Health and Care Excellence (NICE) to develop this guideline.

Guideline Committee

Guideline Development Group

Composition of Group That Authored the Guideline

*Guideline Development Group Members**: Susan Ballard, Lay member, Patient and carer member (June 2012–March 2013); Nicki Doherty, Lead Cancer Manager Rotherham NHS Foundation Trust (January 2012–June 2013), General Manager, Barnsley NHS Foundation Trust (November 2013–present); Jeanne Fay, GP, Oxford; Steve Hajioff (*GDG Chair*) (September 2013–present), Consultant in Public Health Medicine, London; Willie Hamilton (*GDG Clinical Lead*), Professor of Primary Care Diagnostics, University of Exeter; Susan Hay, Patient and carer member; Georgios (Yoryos) Lyratzopoulos, Senior Clinical Research Associate/Honorary Consultant in Public Health, Department of Public Health and Primary Care, University of Cambridge; David Martin, Patient and carer member; Joan Meakins, GP, York; Orest Mulka (*GDG Chair*) (January 2012–June 2013), Retired GP, Derbyshire; Richard Osborne (*GDG Chair*) (July 23-24, 2013 meeting), Consultant Medical Oncologist, Dorset Cancer Centre; Euan Paterson, GP, Glasgow; Liliana Risi, GP, London; Karen Sennett, GP, London; Lindsay Smith, GP, Somerset; Stuart Williams, Consultant Radiologist, Norfolk & Norwich University Hospital

*The Guideline Development Group (GDG) members listed above are those for the 2015 update. For the composition of the previous GDGs, see the full version of the guideline (see the "Availability of Companion Documents" field).

Financial Disclosures/Conflicts of Interest

At the start of the guideline development process all Guideline Development Group (GDG) members' interests were recorded on a standard declaration form that covered consultancies, fee-paid work, share-holdings, research funding (either in the form of programme or project grants or personal research awards), fellowships and support from the healthcare industry. At all subsequent GDG meetings, members declared new, arising conflicts of interest which were always recorded (see Section 4.4 in the original guideline document).

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: National Collaborating Centre for Primary Care. Referral guidelines for suspected cancer in adults and children. London (UK): Royal College of General Practitioners; 2005 Jun. 791 p. [452 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Electronic copies: Available from the National Institute for Health and Care Excellence (NICE) Web site . Also available for download in ePub and eBook formats from the NICE Web site .

Availability of Companion Documents

The following are available:

- Suspected cancer: recognition and referral. Full guideline. London (UK): National Institute of Health and Care Excellence (NICE); 2015 Jun. 378 p. (NICE guideline; no. 12). Electronic copies: Available from the National Institute for Health and Care Excellence (NICE) Web site .
- Suspected cancer: recognition and referral. Full guideline appendices. London (UK): National Institute of Health and Care Excellence (NICE); 2015 Jun. (NICE guideline; no. 12). Electronic copies: Available from the NICE Web site .
- Suspected cancer: recognition and referral. Baseline assessment tool. London (UK): National Institute of Health and Care Excellence (NICE); 2015 Jun. (NICE guideline; no. 12). Electronic copies: Available from the NICE Web site .
- Suspected cancer: recognition and referral. Costing statement. London (UK): National Institute of Health and Care Excellence (NICE); 2015 Jun. 23 p. (NICE guideline; no. 12). Electronic copies: Available from the NICE Web site .
- Suspected cancer: recognition and referral. Costing template. London (UK): National Institute of Health and Care Excellence (NICE); 2015 Jun. (NICE guideline; no. 12). Electronic copies: Available from the NICE Web site .
- The guidelines manual 2012. London (UK): National Institute for Health and Care Excellence (NICE); 2012 Nov. Electronic copies: Available from the NICE Web site .

Patient Resources

The following is available:

- Suspected cancer: recognition and referral. Information for the public. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Jun. 28 p. (NICE guideline; no. 12). Electronic copies: Available from the National Institute for Health and Care Excellence (NICE) Web site . Also available for download in ePub and eBook formats from the NICE Web site . Also available in Welsh from the NICE Web site .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This NGC summary was completed by ECRI on January 17, 2006. The information was verified by the guideline developer on March 15, 2006. This summary was updated by ECRI Institute on August 28, 2015.

The National Institute for Health and Care Excellence (NICE) has granted the National Guideline Clearinghouse (NGC) permission to include summaries of their clinical guidelines with the intention of disseminating and facilitating the implementation of that guidance. NICE has not yet verified this content to confirm that it accurately reflects that original NICE guidance and therefore no guarantees are given by NICE in this regard. All NICE clinical guidelines are prepared in relation to the National Health Service in England and Wales. NICE has not been involved in the development or adaptation of NICE guidance for use in any other country. The full versions of all NICE guidance can be found at www.nice.org.uk .

Copyright Statement

Disclaimer

NGC Disclaimer

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria.

NGC, AHRQ, and its contractor ECRI Institute make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI Institute, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.